Claims

1. A recombinant endolysin comprising or consisting of

(i) a N-terminal catalytic domain~~, or a functional variant thereof~~,

(ii) a C-terminal cell-wall binding region~~, or a functional variant thereof~~, wherein the C-terminal cell-wall binding region comprises or consists of one or more cell-wall binding domains, and

(iii) a linker region between the N-terminal catalytic domain and the C-terminal cell-wall binding region,

wherein the N-terminal catalytic domain is from a first natural endolysin, the linker region and the C-terminal cell-wall binding region are from a second natural endolysin, and wherein the first and the second natural endolysins are encoded by different genomes from different prophages,

~~and~~

wherein said recombinant endolysin has a ~~genus-selective~~ killing activity against *Gardnerella*; and

wherein

(I) the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of any one of SEQ ID NOs: 1 to 5, 7, or 10 to 12, or any variant thereof having at least 80% identity with the amino acid sequence of any one of SEQ ID NOs: 1 to 5, 7, or 10 to 12, whereby said polypeptide or said variant thereof is functional, wherein the function comprises the ability to lyse the cell wall of *Gardnerella*, and

the C-terminal cell-wall binding region comprises or consists of one, two or three cell-wall binding domains, wherein the one, two or three cell-wall binding domains are independently selected from the group consisting of the polypeptides comprising or consisting of the amino acid sequence of SEQ ID NOs: 17 to 24 and 26 to 33, respectively, and any variants thereof having at least 80% identity with the amino acid sequence of SEQ ID NOs: 17 to 24 and 26 to 33, respectively, whereby said polypeptides or said variants thereof are functional, wherein the function comprises the ability to bind to the cell wall of *Gardnerella*; or

(II) the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of any one of SEQ ID NOs: 2 to 5, 7, or 10 to 12, or any variant thereof having at least 80% identity with the amino acid sequence of any

one of SEQ ID NOs: 2 to 5, 7, or 10 to 12, whereby said polypeptide or said variant thereof is functional, wherein the function comprises the ability to lyse the cell wall of *Gardnerella*, and

the C-terminal cell-wall binding region comprises or consists of one, two or three cell-wall binding domains, wherein the one, two or three cell-wall binding domains are independently selected from the group consisting of the polypeptides comprising or consisting of the amino acid sequence of SEQ ID NOs: 15 to 24 and 26 to 33, respectively, and any variants thereof having at least 80% identity with the amino acid sequence of SEQ ID NOs: 15 to 24 and 26 to 33, respectively, whereby said polypeptides or said variants thereof are functional, wherein the function comprises the ability to bind to the cell wall of *Gardnerella*.

~~2. The recombinant endolysin of claim 1 wherein the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of any one of SEQ ID NOs: 1 to 5, 7, or 10 to 12, or any variant thereof having at least 80% identity with the amino acid sequence of any one of SEQ ID NOs: 1 to 5, 7, or 10 to 12, whereby said polypeptide is functional, wherein the function comprises the ability to lyse the cell wall of *Gardnerella*.~~

~~3. The recombinant endolysin of any one of the precedent claims wherein the C-terminal cell-wall binding region comprises or consists of one, two or three cell-wall binding domains.~~

~~4. The recombinant endolysin of claim 3 wherein the one, two or three cell-wall binding domains are independently selected from the group consisting of the polypeptides comprising or consisting of the amino acid sequence of SEQ ID NOs: 15 to 24 and 26 to 33, respectively, and any variants thereof having at least 80% identity with the amino acid sequence of SEQ ID NOs: 15 to 24 and 26 to 33, respectively, whereby said polypeptides are functional, wherein the function comprises the ability to bind to the cell wall of *Gardnerella*.~~

2. A recombinant endolysin comprising or consisting of

(i) a N-terminal catalytic domain,

(ii) a C-terminal cell-wall binding region, wherein the C-terminal cell-wall binding region comprises or consists of one or more cell-wall binding domains, and

(iii) a linker region between the N-terminal catalytic domain and the C-terminal cell-wall binding region,

wherein the N-terminal catalytic domain is from a first natural endolysin, the linker region and the C-terminal cell-wall binding region are from a second natural endolysin, and wherein the first and the second natural endolysins are encoded by different genomes from different prophages,

wherein said recombinant endolysin has a genus-selective killing activity against *Gardnerella*; and

wherein

(II) the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of any one of SEQ ID NOs: 1 to 5, 7, or 10 to 12, or any variant thereof having at least 80% identity with the amino acid sequence of any one of SEQ ID NOs: 1 to 5, 7, or 10 to 12, whereby said polypeptide or said variant thereof is functional, wherein the function comprises the ability to lyse the cell wall of *Gardnerella*, and

the C-terminal cell-wall binding region comprises or consists of one, two or three cell-wall binding domains, wherein the one, two or three cell-wall binding domains are independently selected from the group consisting of the polypeptides comprising or consisting of the amino acid sequence of SEQ ID NOs: 17 to 24 and 26 to 33, respectively, and any variants thereof having at least 80% identity with the amino acid sequence of SEQ ID NOs: 17 to 24 and 26 to 33, respectively, whereby said polypeptides or said variants thereof are functional, wherein the function comprises the ability to bind to the cell wall of *Gardnerella*; or

(II) the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of any one of SEQ ID NOs: 2 to 5, 7, or 10 to 12, or any variant thereof having at least 80% identity with the amino acid sequence of any one of SEQ ID NOs: 2 to 5, 7, or 10 to 12, whereby said polypeptide or said variant thereof is functional, wherein the function comprises the ability to lyse the cell wall of *Gardnerella*, and

the C-terminal cell-wall binding region comprises or consists of one, two or three cell-wall binding domains, wherein the one, two or three cell-wall binding domains are independently selected from the group consisting of the polypeptides

comprising or consisting of the amino acid sequence of SEQ ID NOs: 15 to 24 and 26 to 33, respectively, and any variants thereof having at least 80% identity with the amino acid sequence of SEQ ID NOs: 15 to 24 and 26 to 33, respectively, whereby said polypeptides or said variants thereof are functional, wherein the function comprises the ability to bind to the cell wall of *Gardnerella*.

~~5~~3. The recombinant endolysin of ~~any one of the preceding claims~~claim 1 or claim 2, wherein the C-terminal cell-wall binding region comprises or consists of a first cell-wall binding domain and a second cell-wall binding domain, wherein said first cell-wall binding domain is selected from the group consisting of SEQ ID NOs: 15, 17, 19, 21, 23, 26, 28, 30 and 32 and said second cell-wall binding domain is selected from the group consisting of SEQ ID NOs: 16, 18, 20, 22, 24, 27, 29, 31 and 33.

4. The recombinant endolysin of claim 1 or claim 2, wherein the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 2 and the C-terminal cell-wall binding region comprises or consists of one, two or three cell-wall binding domains, wherein the one, two or three cell-wall binding domains are independently selected from the group consisting of the polypeptides comprising or consisting of the amino acid sequence of SEQ ID NOs: 28 to 33.

5. The recombinant endolysin of claim 1 or claim 2, wherein the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 7 and the C-terminal cell-wall binding region comprises or consists of one, two or three cell-wall binding domains, wherein the one, two or three cell-wall binding domains are independently selected from the group consisting of the polypeptides comprising or consisting of the amino acid sequence of SEQ ID NOs: 19 and 20.

6. The recombinant endolysin of claim 1 or claim 2, wherein the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 2 and the C-terminal cell-wall binding region comprises or consists of a first cell-wall binding domain and a second cell-wall binding domain, wherein said first cell-wall binding domain is selected from the group consisting of the polypeptides comprising or consisting of an amino acid sequence having at least 90% identity with the amino acid

sequence of any one of SEQ ID NOs: 28, 30 and 32, and said second cell-wall binding domain is selected from the group consisting of the polypeptides comprising or consisting of an amino acid sequence having at least 95% identity with the amino acid sequence of any one of SEQ ID Nos: 29, 31 and 33, and wherein said first and second cell-wall binding domains are functional and the function comprises the ability to bind to the cell wall of *Gardnerella.*

7. The recombinant endolysin of claim 1 or claim 2, wherein the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 2 and the C-terminal cell-wall binding region comprises or consists of a first cell-wall binding domain and a second cell-wall binding domain, wherein said first cell-wall binding domain is selected from the group consisting of SEQ ID NOs: 28, 30 and 32, and said second cell-wall binding domain is selected from the group consisting of SEQ ID NOs: 29, 31 and 33.

8. The recombinant endolysin of claim 1 or claim 2, wherein the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 2 and the C-terminal cell-wall binding region comprises or consists of a first cell-wall binding domain and a second cell-wall binding domain, wherein said first cell-wall binding domain is defined by SEQ ID NO: 28 and said second cell-wall binding domain is defined by SEQ ID NO: 29.

9. The recombinant endolysin of claim 1 or claim 2, wherein the N-terminal catalytic domain is a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 2 and the C-terminal cell-wall binding region comprises or consists of a first cell-wall binding domain and a second cell-wall binding domain, wherein said first cell-wall binding domain is defined by SEQ ID NO: 28 and said second cell-wall binding domain is defined by SEQ ID NO: 31.

~~6~~10. The recombinant endolysin of any one of claim ~~5~~s 3 and 6 to 9, wherein said first cell-wall binding domain is N-terminally of said second cell-wall binding domain.

~~7~~11. The recombinant endolysin of any one of the precedent claims wherein the linker region is a polypeptide comprising or consisting of the amino acid sequence:
(i) (XXX)n, wherein each X can be independently G, A or S, preferably wherein the amino acid sequence (XXX)n is (GGS)n, wherein n corresponds to the number of repetitions of the sequence XXX, preferably wherein n is 2, 3, 4, 5 or 6; or
(ii) $X_1X_2GLNGX_3X_4NGGS$, wherein X_1 is N or K, X_2 is A or V, X_3 is Y or C and X_4 is K or Q.

12. The recombinant endolysin of claim 1, wherein said endolysin has a genus-selective killing activity against *Gardnerella.*

~~8~~13. The recombinant endolysin of any one of the precedent claims wherein said endolysin has a killing activity against *Gardnerella vaginalis sensu stricto, Gardnerella leopoldii, Gardnerella piotii* and/or *Gardnerella swidsinskii,* or any other species in the genus *Gardnerella*.

~~9~~14. The recombinant endolysin of any one of the precedent claims wherein said endolysin has no killing activity against *Lactobacilli*~~.~~.

15. The recombinant endolysin of any one of the precedent claims, ~~preferably~~ wherein said endolysin has no killing activity against *Lactobacilli crispatus*, *Lactobacilli gasseri*, and/or *Lactobacilli jensenii*.

~~10~~16. A polynucleotide which encodes the recombinant endolysin of any one of claims 1 to ~~9~~15.

~~11~~17. A pharmaceutical composition comprising the recombinant endolysin of any one of claims 1 to ~~9~~–15 or the polynucleotide of claim ~~8~~–16 and further comprising a pharmaceutically acceptable carrier and/or diluent.

~~12~~18. A recombinant endolysin as defined in any one of claims 1 to ~~9~~15, a polynucleotide as defined in claim ~~10~~ 16 or a pharmaceutical composition as defined in claim ~~11~~ 17 for use in treating a disease or disorder.

~~13~~19. ~~The recombinant endolysin for use according to claim 12~~1, ~~the polynucleotide for use according to claim 12~~ 1 ~~or the pharmaceutical composition for use according to claim 12~~ 1 ~~wherein said disease or disorder is~~ Use of a recombinant endolysin as defined in any one of claims 1 to 15, a polynucleotide as defined in claim 16 or a pharmaceutical composition as defined in claim 17 in the manufacture of a medicament for treating a bacterial infection caused by at least one strain of the *Gardnerella* genus.

~~14~~20. ~~The recombinant endolysin for use according to claim 13~~1, ~~the polynucleotide for use according to claim 13~~ 1 ~~or the pharmaceutical composition for~~ The use according to claim ~~13~~ 19 wherein said bacterial infection is bacterial vaginosis.

~~15~~21. ~~The recombinant endolysin for use according to claim 14, the polynucleotide for use according to claim 14 or the pharmaceutical composition for~~ The use according to claim ~~14~~ 20 wherein said bacterial vaginosis is caused by *Gardnerella vaginalis sensu stricto, Gardnerella leopoldii, Gardnerella piotii* and/or *Gardnerella swidsinskii*.

~~16~~22. ~~The recombinant endolysin for use according to any one of claims 13 to 15~~1 ~~to 2~~, ~~the polynucleotide for use according to any one of claims~~ 1 ~~to 2~~13 ~~to 15 or the pharmaceutical composition for~~ The use according to any one of claims 19 to 21, ~~13 to 15~~ wherein said ~~recombinant endolysin, polynucleotide or pharmaceutical composition~~ medicament is to be administered locally, preferably wherein said ~~recombinant endolysin, polynucleotide or pharmaceutical composition~~medicament is to be administered locally into the vagina of a female subject and/or into or on the glans penis, prepuce or urethral entry of a male subject.

~~17~~23. ~~The recombinant endolysin for use according to any one of claims~~ 1 ~~to 2~~13 ~~to 15, the polynucleotide for use according to any one of claims~~ 1 ~~to 2~~ 13 ~~to 15 or the pharmaceutical composition for~~ The use according to any one of claims 19 to 22, ~~13 to 15~~

wherein said ~~recombinant endolysin, polynucleotide or pharmaceutical composition~~ medicament is to be administered into the vagina of a female subject and/or into or on the glans penis, prepuce or urethral entry of a male subject.

~~18~~24. ~~The recombinant endolysin for use according to any one of claims 1 to 2~~13 to 17, ~~the polynucleotide for use according to any one of claims 1 to 2 13 to 17 or the pharmaceutical composition for~~ The use according to any one of claims 19 to 23, ~~13 to 17~~ wherein said ~~recombinant endolysin, polynucleotide or pharmaceutical composition~~medicament is to be co-administered with a compound or composition which adjusts the pH of the vagina to 4.0 – 6.0.

~~19~~25. A plasmid comprising the polynucleotide of claim ~~10~~16.

~~20~~26. A bacterial host cell comprising the plasmid of claim ~~19~~25, preferably wherein the bacterial host cell is an *E. coli* cell.

~~21~~27. An *in vitro* method for the diagnosis of a disease or condition which can be treated with the endolysin according to any one of claims 1 to ~~9~~15, the method comprising the steps of:

(i) contacting a sample obtained from the subject with a polypeptide comprising or consisting of the C-terminal cell-wall binding region of the endolysin according to any one of claims 1 to ~~9~~15, and optionally the N-terminal catalytic domain of the endolysin according to any one of claims 1 to ~~9~~15, wherein the sample comprises microbial cells, and wherein the C-terminal cell-wall binding region of said endolysin is optionally labelled;

(ii) testing whether the polypeptide binds to, and/or lyses, the microbial cells of the sample; and

(iii) determining that a disease or condition can be treated with the endolysin according to any one of claims 1 to ~~9~~ 15 if the polypeptide binds to, and/or lyses, the microbial cells.